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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,684	10/27/2003	Tetsuya Suga	242791US0CONT	2064

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EXAMINER	
BRANSON, DANIEL L	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/692,684	SUGA ET AL.	
	Examiner	Art Unit	
	DANIEL L. BRANSON	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *36,39-42,44-46 and 91-95* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *36, 39-42, 44-46 and 91-95* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 24, 2011 has been entered.

Status of Application

Claims 36, 39-42, 44-46 and 91-94 are currently pending. Claims 39 and 44 are currently amended, claims 1, 12-17, 19, 20, 22-35, 48-53 and 75-78 were cancelled and claims 91-94 were newly added.

Receipt and consideration of Applicants amendments and remarks filed on October 24, 2011 is acknowledged.

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are reiterated. They constitute the complete set of rejections presently being applied to the instant application.

The examiner assigned to this case has changed. Please make a note of the change for future correspondence.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 36, 39-42, 45-46 and 91-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0119164 A1 to Uchiyama et al., in view of JP 11-262370 A to Miyabayashi et al., US 6,858,214 B1 to Kropf et al. and the article entitled "Gastrointestinal Uptake of biodegradable microparticles: Effect of particle size" by Desai et al. as evidenced by the article entitled "structural characterization of a water-soluble β-D-glucan from fruiting bodies of *Agaricus blazei Murr*" by Dong et al. and the article entitled "Potentiation of intestinal immunity by micellary mushroom extract" by Shen et al.

Applicant Claims

Applicant claims a process for producing superfine particles comprising superfine pulverizing a β-glucan derived from a water extract of a mushroom, by mixing the aqueous solution containing the β-glucan derived from a water extract of a mushroom with a high pressure dispersant, such as lecithin and thereafter homogenizing the mixed composition at a pressure of 800 kgf/cm^2.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Uchiyama et al. teach Agaricus blazei (a mushroom) in whole, particulate, or extracted form, can be used to treat forms of damage to the skin caused by toxins and chemicals (abstract, para [0025]). Agaricus blazei (a mushroom) in whole, particulate, or extracted form, when taken internally, also offers protection against various disorders including autoimmune disorders (abstract, para [0026]). The identified compounds that have been extracted from Agaricus blazei and that are of particular use in the invention include beta glucans (para [0034] claims 1 and 12).

The extraction can be done by immersing particulate Agaricus blazei in plain hot water, preferably over 90℃ (para [0032]-[0033]). The extract may be freeze dried or concentrated using water or methanol/acetone solutions (para [0033]). The ratio of mushroom to water is preferably between1:2 and 1:100 (para [0033]). The concentration of the extract is preferably between 0.05% and 50% v/v (para [0044]). The extract can be further filtered using gel permeation (para [0033]).

The hot water extract of Agaricus blazei necessarily contains beta glucan. As evidence of this, the Patent Examiner cites the article entitled "Structural characterization of a water soluble β-D-glucan from fruiting bodies of *Agaricus blazei* Murr" by Dong et al. Dong et al. teach β-D-glucan was obtained in a hot-water (100 ˚C) extract of the fruiting bodies of *Agaricus blazei* and then further isolated by ethanol precipitation, anion-exchange and gel-permeation chromatography (abstract, pg 1420, para 4-6). As Uchiyama teaches the hot water extraction protocol on *Agaricus blazei*

preferably uses water which is above 90 °C and up to 100 °C, the extract obtained thereby would necessarily contain β-glucans as indicated by Dong et al. Thus, Uchiyama necessarily teaches a composition comprising particles of a β-glucan derived from a water extract of a mushroom.

The extract can be mixed with other active or inactive ingredients and can be formulated as an emulsion (para [0045], [0051]). These ingredients may include agents (dispersants) added to the preparation to produce better dispersions (para [0045], [0051]).

The extract is useful for treating skin disorders and internal diseases such as autoimmune diseases topical or internally (orally) (para [0037]-[0043], [0048]-[0049]). The extract may treat diabetes, lupus, certain types of cancer and can be used in the form of a food, drink or dietary product (para [0050]).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Uchiyama et al. teach the Agaricus blazei extract (i.e. beta glucans) can be present in particulate form but do not explicitly teach the particle size or that this size is obtained through mixing at 800 kgf/cm^2. Uchiyama et al. also do not teach the dispersant is lecithin. These deficiencies are cured by the teachings of Miyabayashi et al., Kropf et al. and Desai et al.

Miyabayashi et al. teach a method of ultrafine pulverizing a composition

comprising Agaricus blazei mushroom which is capable of producing 0.005-0.5 μm particles (para [0001], [0013]). Miyabayashi et al. teach that by preparing ultrafine Agaricus blazei particles this way, the active ingredient is more effectively utilized (para [0001]). The process involves the use of 10 to 150 MPa of pressure (102-1530 kgf/cm^2) to rapidly mix/collide the particles in a fluid to minimize their diameters (para [0022], [0040]). Miyabayashi et al. also teaches that the reduced particle size from Agaricus blazei extract composition produced by the taught method has improved anticancer properties (para [0063]-[0066]).

Kropf et al. teach the use of nanoscalar water-soluble 1,3 beta-glucans. The beta- glucans are contained in cosmetic and/or pharmaceutical preparation having particle diameters in the range of 10 to 300 nm (equivalent to 0.01 to 0.30 μm) (see column 1, lines 43- 47). The composition can further contain adjuvants known in the cosmetic and/or pharmaceutical industry (see column 3, lines 19- 34). Kropf et al. further teach that it is beneficial to utilize an emulsifier when preparing the compositions in order to ensure that the nanoparticles do not agglomerate and to ensure the particles maintain their small diameter (column 2, lines 23-27). Kopf et al. teach that lecithin can be used in the composition as a hyperfatting agent (emulsifier) (column 5, lines 51-52).

Desai et al. teach the effect of particle size on the gastrointestinal uptake of biodegradable microparticles. In general, the efficacy of uptake of 100nm size microparticles by the intestinal tissue (e.g. Peyer's patch) was 15-250 folds higher when compared to large size microparticles. This is particularly important in the design of oral

drug delivery systems (see the abstract).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention by applicant to utilize the method of obtaining superfine particles of Agaricus blazei mushroom as taught by Miyabayashi et al. on the beta glucan particle water extracts from Agaricus blazei mushroom taught by Uchiyama et al. because both references are directed to compositions comprising particles from the same mushroom that have the same anticancer pharmaceutical effect. Furthermore, an ordinarily skilled artisan would have been motivated to utilize the superfine pulverizing method of Miyabayashi et al. on the particles of Uchiyama et al. because doing so would have resulted in an increased delivery of the active to the intestinal tissue and resultant utilization as taught by Desai et al. and Miyabayashi et al.

It would further have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention by applicant to combine the teachings of Kropf et al. with those of Uchiyama et al. because Kropf solves a problem that was known in the art of pharmaceutical nanoparticle suspensions. *KSR International Co. v. Teleflex Inc., et al.*, 550 U.S. 398 (2007). Specifically, Kropf et al. teach that it is important to utilize an emulsifier with nanoparticles to prevent agglomeration and the resultant increase in particle size when suspending nanoparticles in an aqueous formulation. Thus, it would

have been obvious to one of ordinary skill in the art to utilize any of the emulsifiers in Kropf et al., including lecithin, in the combined method of Uchiyama et al. and Miyabayashi et al. in order to prevent the nanoparticle produced in the combined method from agglomerating, such agglomeration having reduced the absorption and effectiveness of the composition. Furthermore, because beta-1,3-glucan is the major component of yeasts and mushrooms which would have inherently been contained in the hot water extract of Uchiyama et al. (see Shen et al. pg 71, col 2, para 3; pg 76, col 1, para 3), one of ordinary skill in the art to would have had an expectation of successful results in combining these teachings of Kropf et al. with those of Uchiyama et al.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed October 24, 2011 have been fully considered but they are not persuasive. Applicant argues that the primary reference Uchiyama et al., is overly generic and does not actually disclose or suggest that the water extract of mushroom Agaricus blazei contains any β-glucans, nor that the specific fractions containing β-glucans could or would be used for any specific purpose.

This argument is not persuasive for three reasons. First, Uchiyama et al. specifically teaches that extracts of Agaricus blazei are preferably prepared using "water

extraction" or more preferably "hot water extraction" (see paragraphs 32 and 33). Identified compounds in polar solvent extracts include beta-glucans (see paragraph 34). Thus, it would have been obvious to one of ordinary skill in the art to try water extraction or hot water extraction to obtain beta glucans since they are preferred methods in obtaining the polar solvent extracts of identified compounds (i.e. beta glucans). Second, water is a more polar solvent than methanol, thus hot water extracts of *Agaricus blazei* would necessarily contain β-glucans which contain many polar hydroxyl groups. To provide additional evidence/basis in fact to demonstrate that hot water extracts of Agaricus blazei inherently and necessarily contain beta-glucans as asserted, the Patent Examiner cites the article entitled "Structural characterization of a water soluble β-D-glucan from fruiting bodies of *Agaricus blazei* Murr" by Dong et al. Dong et al. teach β-D-glucan was obtained in a hot-water (100 ˚C) extract of the fruiting bodies of *Agaricus blazei* Murr which was then further isolated by ethanol precipitation, anion-exchange and gel-permeation chromatography (abstract, page 1420, paragraphs 4-6). As Uchiyama teaches the hot water extraction protocol on *Agaricus blazei* preferably uses water which is above 90 ˚C and up to 100 ˚C, the extract obtained thereby would necessarily contain β-glucans as indicated by Dong et al. Thus, Uchiyama necessarily teaches a composition comprising particles of a β-glucan derived from a water extract of a mushroom. Third, Applicant has chosen to claim the invention as a composition and a method of making that composition, not a method of using the composition. Thus, arguments alleging that Uchiyama et al. do not suggest a specific purpose for the β-glucans are irrelevant. After giving the Applicant's claims their broadest reasonable

interpretation, no intended use is required by the limitations of the claims. Even if the claims did require the composition to be used for a specific purpose, Uchiyama et al. teach that their hot water extract of mushroom, which would necessarily comprise β-glucan as established above, can be used topically to prevent and treat damage to skin such as skin cancers and can be taken internally to treat or prevent disorders such as diabetes.

Applicants further argue that Kropf et al. teach the particle size of a yeast extract of beta- glucans and not mushroom extracts of beta-glucans, and thus is related to a different invention. Applicant argues that beta glucans extracted from yeast are structurally different. Applicant has provided references to establish that beta glucans derived from yeast are structurally different from beta glucans extracted from mushrooms. Applicant has further provided a declaration from Yasuyo Suga where Yasuyo has opined that because of the differences in structure between the β-glucans derived from mushrooms and yeast, a skilled artisan would not modify a disclosure of β-glucans from one based on a disclosure of β-glucans from the other.

Applicant's argument of non-analogous art is not convincing. First and foremost, Applicant claims a β-glucan derived from a water extract of a mushroom, without limiting to a β(1→6) glucan. The attempt to distinguish the β-glucan structurally by source additionally fails because Applicant cannot prove hot water extracts of mushrooms are void of β(1→3) glucans, the type of β-glucans found in yeast. Indeed, one of the references that Applicant has provided to this Office states in part, "Primarily, β-1,3-glucan is the major component of oats, mushrooms and yeasts" ('Potentiation of

intestinal immunity by micellary mushroom extracts' by Shen et al). Thus, trying to distinguish the reference based upon structure fails. Furthermore, the expert opinion of Yasuyo Suga sets forth facts which are incomplete with the prior art as cited above by ignoring the fact that a major component of the β-glucans of both mushrooms and yeast are β(1→3)glucans. Thus, the opinion and conclusion derived therefrom is found unpersuasive.

Even if the claim had limited the β-glucan to a β-(1→6)-glucan, β-glucans from both mushrooms and yeast are known in the art to possess immune modulation activities. A skilled artisan looking to enhance the absorption, bioavailability and degree of immune activation of and by a mushroom β-glucan would have been motivated to look to at least the prior art of β-glucans, regardless of source, to obtain a solution to the enumerated problems to be solved and would have found Kropf et al. Although Kropf et al. teach that the beta glucans are prepared from a yeast extract, the end result is the same. In both references, the beta glucans are being used for the same purpose and in the same type of formulations. It would have been obvious to one of ordinary skill in the art to try to prepare the beta glucans taught in Uchiyama et al. within the same particle size range as instantly claimed (i.e. less than 10 microns) because it has been disclosed by Kropf et al. that beta glucans can be used effectively in cosmetic and pharmaceutical formulations when prepared within the instantly claimed particle size range (i.e. less than 10 microns). Furthermore, while Applicant has repeatedly pointed out that some yeast and mushroom β-glucans differ structurally, they have failed to provide evidence that these structural differences actually make the mushroom β-

glucans less suitable for forming superfine particles utilizing the method of Kropf et al which would discourage a skilled artisan from relying on Kropf et al. to solve these problems. Indeed, such a showing would be difficult in the light of the fact that the method of Kropf et al. is very similar to that of Applicant used to prepare the instantly claimed particles of β-glucan derived from a water extract of a mushroom. Finally, it is known in the art that a smaller particle size (e.g. 100 nm) has a higher efficiency of uptake when compared to larger particle sizes, as suggested by Desai. The particulate carrier system is important for oral drug delivery in order to enhance absorption and bioavailability.

Next the Applicant defers to three declarations in order to attempt to establish non-analogous art as well as secondary considerations/unexpected results in which to overcome the present *prima facie* case of obviousness. Each of the three declarations will be discussed below in turn and conclusions regarding probative value regarding the establishment of unexpected results and non-analogous art are reiterated from past office actions as well as issued de novo.

Consideration of §1.132 Declarations

A Declaration is reviewed for at least the following: 1) whether there is a nexus between the merits of the claimed invention and the evidence of secondary considerations (*Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 227 USPQ 657,673-674 (Fed. Cir. 1985)), 2)* whether the declaration compares the claimed subject matter with the closest prior art (*In re Burckel*, 201 USPQ 67 (CCPA 1979)), 3) whether the objective evidence of non-obviousness is commensurate in scope with the claims

which the evidence is offered to support (*In re Clemens,* 206 USPQ 289, 296 (CCPA 1980)), 4) whether the Declaration shows a difference in kind rather than merely a difference in degree (*In re* Waymouth, 182 USPQ 290, 293 (CCPA 1974)), and 5) whether the record establishes such a strong case of obviousness that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness (*Newell Cos. V. Kenney Mfg. Co.* 864 F.2d 757, 769; *Richardson-Vicks, Inc., v. The Upjohn Co.,* 122 F.3d 1476, 1484). The Patent Examiner must also determine whether the evidence shows unexpected results (MPEP 716.02(a)).

Applicant has submitted a § 1.132 declaration on September 23, 2009. Applicant compared a beta-glucan solution wherein beta-glucan has an average diameter of about 200 microns, a beta-glucan solution wherein beta-glucan has an average diameter of about 100 nm (instant invention), and a control where no beta-glucan is used. The compositions were evaluated for incorporation (absorption) into the small intestines Peyer's patch. The composition of the instant invention (solution of beta-glucan with a particle size of about 100 nm) had the highest absorbability.

First, it should be noted that figures 1, 3, 5 are not visible and figures 2, 4, 6 are not in color. And thus, one of ordinary skill in the art cannot visibly and accurately ascertain whether any unexpected results have occurred with respect to the photographs.

Second, Applicants have not compared their invention with the closest prior art, but rather with beta-glucan particle of a 200 micron diameter. Thus, with no gauge of

how absorption into peyer's patches was different from that of the closest prior art, unexpected results cannot be ascertained.

Finally, Applicant is purporting that the use of beta-glucans with a superfine particle size resulted in a higher absorbability. However, this result is not unexpected. It is known in the art that particle size plays a role in the gastrointestinal uptake of drugs or carriers and the use of smaller "superfine" particle sizes (e.g. 100 nm) will lead to an increase in uptake of particles in tissues, such as Peyer's patch, when compared to the use of larger particles sizes (as evidenced by Desai et al.). Thus, it is not unexpected for a solution containing beta-glucan at a particle size of 100 nm to be absorbed by the intestinal tissue in a greater amount when compared to the beta-glucan solution having a beta-glucan particle size of 200 microns.

Applicant has submitted another two § 1.132 declarations on September 27, 2010 and April 21, 2011. It should be noted these declarations consist of opinion. Opinions directed to legal conclusions are not considered and are given no weight whereas opinions directed to technical data are considered but given reduced weight.

In the declaration of September 27, 2010, Applicant has given an opinion that a skilled artisan would not modify a disclosure of β-glucans from mushrooms based on a disclosure of β-glucans from yeast. The opinion is based on the fact that there are various types of β-glucans, and there are differences in structure between β-glucans from mushrooms and those from yeast. Applicant argues that mushrooms, but not yeast, contain β-1,6-glucans. To support the proposition that mushrooms contain β-1,6-glucans, Applicant cites 5 articles that study separately the compositions of three

different mushrooms, Lentinula edodes, Schizophyllum commune and Selerotium. Applicants cite several entries from wikipeida.org as well as two other references to show that yeast comprise mostly β-glucans having 1,3 linked mains chains and partly having 1,6 linked branched chains and that mushrooms comprise the 1,6 linked main chains, not the 1,6 linked branched chains.

The Patent Examiner, after considering this portion of the Declaration and articles, accepts at face value that mushrooms contain some β-glucans which yeast do not. That some β-glucans are different between the different sources, however, is not the end of the inquiry. Investigation must also be made into the portion of β-glucans which are similar or the same between the different sources. Indeed, Applicant admits that both yeast and mushrooms contain β-1,3-glucans in the present Declaration (see page 2, paragraph 1) and has presented a reference to this Office in this Declaration that says in part, "Primarily, β-1,3-glucan is the major component of oats, mushrooms and yeasts" ('Potentiation of intestinal immunity by micellary mushroom extracts' by Shen et al). Thus, as the prior art is clear that a majority of β-glucans in mushrooms and yeast are β-(1,3)-glucans, the Declarants conclusion of non-analogous art based upon incomplete facts is given reduced weight.

The declarant further asserts that there is no direct relationship between the absorbability and the medical effect of β-glucans and points to two Suga et al. and one Shen et al. reference to support this proposition. Possible explanations are given for why particle size is not always directly related to absorbability and immune activation by the active agent. Despite the previous declaration's lack of evidence as to medical

effect or immune activation induced by the particle, Declarant then concludes that the absence of a direct link between absorbability and the medical effect of β-glucan proves that the results demonstrated in the previous Declaration (which increased absorbability) are unexpected.

The Patent Examiner has reviewed both of the Suga et al references as well as the Shen et al. reference. The only reference which provides objective evidence to support the Applicants conclusion that absorbability/size of the β-glucan is not directly related to the medical effect thereof is the Suga et al. reference published in 2005. In Suga et al (2005), it was demonstrated that oral administration of M-LNT and MME particles approximately 0.4 microns in diameter induced anti-tumor activity, while L-LNT of approximately 130 microns and S-LNT of an unmeasurably small diameter did not (the latter which was presumed to be absorbed in the GI tract because of its small diameter). The Patent Examiner finds this objective evidence as an indication of unexpected results regarding medicinal effects of the particle size of M-LNT as compared with similarly prepared, but larger/smaller diameter L-LNT and S-LNT.

This objective evidence, however, must be considered in light of factors 2) and 3) *supra*. Suga et al. (2005) does not compare M-LNT against the closest prior art. Thus, with no gauge of how the medical effect of certain sized particles was different from that of the closest prior art, unexpected results cannot be ascertained in this regard. Furthermore, Suga et al's objective evidence of non-obviousness is not commensurate in scope with the claims which the evidence is offered to support. The independent claims of issue require that the particles of β-glucan are less than 10 microns. Suga et

al (2005) clearly demonstrates that not all particle less than 10 microns exhibit a medical effect. It is difficult to ascertain where the line is drawn, as the smallest particle that exhibited no medical effect has an undetermined diameter. Nonetheless, the claim limitation regarding particle size is much broader than the 0.4 micron diameter which has been demonstrated to have unexpected results in Suga et al (2005).

It should also be noted that the assertion made in the first Suga declaration regarding the exertion of an inhibitory effect on tumor growth being dependent on particle diameter, and that smaller particle size is absorbed into peyer's patch and larger particles are not is completely at odds with the assertion in the second Suga declaration that there is no direct relation between particle size, absorption and medical effect of the β-glucan particle.

Applicant filed a third Declaration on April 21, 2011. Essentially the results of Suga et al. (2005) were outlined and Dr. Okumura concluded that a correlation between the particle size and the effects of β-glucan cannot be predicted and would not have been expected. In order to avoid duplicity, the Patent Examiner directs the Applicant's attention to the above discussion of Suga et al. (2005) which addresses the salient points of this third Declaration.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Patent Examiner should be directed to DANIEL L. BRANSON whose telephone number is (571)270-3812. The Patent Examiner can normally be reached on M-F 7-3:30.

If attempts to reach the Patent Examiner by telephone are unsuccessful, the Patent Examiner's supervisor, Johann R. Richter can be reached on (571)272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel L. Branson
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/Johann R. Richter/

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